

### Amendments to the Specification:

Please replace the paragraph at page 3, line 18 to page 4, line 4 with the following paragraph:

ICAT has a number of shortcomings. First, ICAT only comes in two masses (light and heavy) that differ by just 8 mass units, but there are applications that require comparisons of more than three or even more states, not just two. Second, cysteine (Cys) is one of the least abundant amino acids. For example, the frequency of arginine is about 5.6% compared to the frequency of cysteine, which is about 2.2%. See Figure 1. Indeed, about 97% of the sequences contained in the GenBank® database (<http://www.ncbi.nlm.nih.gov/>) contain arginine while only 84.7% contain cysteine. Thus, more than 15% of such sequences would be outside the scope of a method that targeted cysteine. Furthermore, cysteine is even more underrepresented in proteins/peptides smaller than 10 kDa or 5 kDa (only ~80% or 57%, respectively, contain Cys) and totally absent in many classes of signaling molecules such as short peptide hormones and neurotransmitters (e.g., dynorphins, enkephalins, substance P, vasoactive intestinal peptide, LHRH, growth hormone-releasing hormone, glucagons-like peptide, bradykinin, angiotensin, etc.). Third, the deuterium mass tags add a number of steps to ICAT synthesis, making the reagent slow and expensive to prepare, prohibitively so in large quantities. Fourth, the iodoacetamide moiety is not the best Cys-reactive moiety. It has a preference for Cys, but can also react with methionine and histidine. See Haugland et al., "Handbook of Fluorescent Probes and Research Chemicals," 6<sup>th</sup> Ed., 49-50 (1996). Furthermore, the iodoacetamide reactive group is unstable in light and can result in more than one product with Cys, thus generating heterogeneity and complicating the bioinformatics analysis.